IN THE SPECIFICATION:

Please amend the specification as follows:

Page 1, line 19, insert:

--This application is a continuation application of U.S. application no. 08/327,874 filed October 24, 1994 and now ~~pending~~ US 6,372,249, which is a continuation-in-part of PCT/US94/09700 filed August 26, 1994 and now abandoned, which is a continuation-in-part of U.S. application no. 08/274,535 filed July 13, 1994 and now abandoned, which is a continuation-in-part of U.S. application no. 08/229,420 filed April 15, 1994 and now abandoned, which is a continuation-in-part of U.S. application no. 08/203,535 filed February 25, 1994 and now abandoned, which is a continuation-in-part of U.S. application no. 08/153,564 filed November 17, 1993 and now abandoned, which is a continuation-in-part of U.S. application no. 08/113,372 filed August 30, 1993 and now abandoned, which is a continuation-in-part of U.S. application no. 07/970,462 filed November 2, 1992 and now U.S. Patent No. 5,302,706, and divisional U.S. application nos. 08/160,814 filed January 3, 1994 and now U.S. Patent No. 5,424,400 and U.S. application no. 08/268,439 filed June 30, 1994 and now abandoned, all of which are continuations-in-part of U.S. application no. 07/808,523 filed December 16, 1991 and now abandoned.--

IN THE CLAIMS:

Please add the following new claim 21.

--21. An antibody capable of binding senescent cell derived-1, SDI-1 comprising the amino acid sequence 60 through 164 of SEQ ID NO:2.--

REMARKS

The claims have been amended to define Applicants' invention with greater particularity and to set forth the invention in such manner as to clearly demonstrate its patentability over the art. New claim 21 is directed to subject matter found in the specification as originally filed in the '874 patent application (filed October 24, 1994).

In the present invention, a high affinity polyclonal antibody to a GST fusion protein of SDI-1 was generated and methods of detection using that antibody are described in the specification on pages 45 to 48. Thus, no new matter is added with this preliminary amendment. The polyclonal antibody to a GST fusion protein of SDI-1 of this application is currently being commercialized as p23, which is indicia of non-obviousness of the instantly claimed invention.

Practical Approach. IRL Press, Oxford, England, pp. 143-164 (1985), herein incorporated by reference).

EXAMPLE 3

cDNA CLONING OF THE SENESCENT CELL DERIVED INHIBITORS (SDI) OF DNA SYNTHESIS

Double-stranded cDNAs were synthesized from senescent cell derived poly A+ RNA, which has been shown to inhibit DNA synthesis in young cells when microinjected into the cytoplasm (Lumpkin, C.K. *et al.*, *Science 232*:393-395 (1986)). The cDNAs were size fractionated, inserted into pcDSRαΔ The resulting E. coli clones were divided into small pools. Plasmids from each pool were co-transfected with the transfection marker plasmid, pCMVβ, which allowed a determination of the labelling index of transfected cells specifically, since even in high efficiency transfection, frequencies varied from experiment to experiment. Transfection frequencies of the marker plasmid ranged from 30-90%. About 200 cDNA pools were screened and four pools remained positive for DNA synthesis inhibitory activity after five repeated transfections. The candidate pools were then divided into individual plasmids and screened further.

Three independent positive plasmid clones were obtained. In the cDNA pool A, only one plasmid, No. 2, exhibited strong DNA synthesis inhibitory activity. Similarly, in pools B and C only one cDNA clone caused inhibition. The size of inserted cDNAs was 2.1 kb, 1.2 kb and 2.7 kb, respectively. These cDNA sequences have been designated as senescent cell derived inhibitors, SDI-1, SDI-2 and SDI-3, respectively.

The nucleotide sequence of the SDI-1 cDNA clone (SEQ ID NO: 1), and the amino acid sequence of SDI-1 (SEQ ID NO: 2) have been determined. The cDNA sequence presented herein for SDI-1 differs from that described in U.S. Patent Application serial no. 07/808,523 (now abandoned) in possessing an unrecited G at position 286, and in having the sequence CG rather than GC at position 1843-1844. The presently disclosed sequence was obtained through the re-sequencing of the pcDSRαΔ-SDI-1 plasmid whose isolation and

characteristics were described in U.S. Patent Application serial no. 07/808,523 (now abandoned). *E. coli* DH5 transformed with the pcDSRαΔ-SDI-1 plasmid was deposited with the American Type Culture Collection, Rockville, Maryland, USA, on October 1, 1992, and has been accorded accession number ATCC 69081.

A nucleic acid molecule whose sequence corresonds to a portion of the SDI-1 nucleotide sequence reported herein has been identified among the 2375 random gene sequence fragments reported by Adams, M.D. *et al.* (*Nature 355*:632-634 (1992)).

EXAMPLE 4

MICROINJECTION OF SDI SEQUENCES INTO YOUNG CYCLING CELLS

In order to verify the functional activity of SDI sequences, microinjections were performed. A plasmid carrying either SDI-1 or SDI-2 was co-microinjected with the marker plasmid into the nuclei of young cycling cells. The labelling index of the resulting blue cells was determined (Table 1). These plasmids showed strong inhibitory activity on DNA synthesis of young cells. For control experiments, the empty vector was co-microinjected with the marker plasmid. This caused slight inhibition when the labelling index was compared with uninjected cells, a phenomenon also observed in transfection experiments. Microinjections with SDI-3 were not performed because the inhibitory activity was lower than SD-I and SD-2 transfection experiments.

In addition to normal human fibroblasts, the SDI-1 molecules were also found to be capable of inhibiting the synthesis of DNA in several tumor cell types (melanoma, lung carcinoma, and ovarian tumor), and in immortalized SV40-transformed fibroblasts, and CHO cells. SDI-1 molecules were also capable of inhibiting the synthesis of DNA in normal bovine pulmonary artery smooth muscle.